

REMARKS

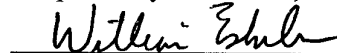
The specification has been amended to delete non-ASCII files from the Computer Program Listing Appendix and to insert sequence ID numbers. Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version with markings to show changes made."

Please delete the Computer Program Listing Appendix submitted with the original application and enter the enclosed Computer Program Listing Appendix contained on two identical compact discs. A separate transmittal letter for the compact discs is enclosed. No new matter has been added.

Also enclosed are 1) a paper copy of the initial "Sequence Listing"; 2) an computer readable form of the initial "Sequence Listing" on a 3.5" floppy disk; and 3) a statement that the content of the sequence listing information recorded in computer readable form is identical to the written sequence listing and contains no new matter. Please enter the enclosed initial "Sequence Listing" in the application.

Should there be any questions regarding this application, the examiner is invited to contact the undersigned attorney at the number shown below.

Respectfully submitted,



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Date: April 30, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Paragraph beginning at page 1, line 10 has been amended as follows:

## REFERENCE TO COMPUTER PROGRAM LISTING APPENDIX

A Computer Program Listing Appendix is hereby expressly incorporated by reference. The Computer Program Listing Appendix includes two duplicate compact discs. The files on each compact disc, the date created and the file size in bytes are:

| <u>File Name</u>                                 | <u>Date Created</u> | <u>Size (bytes)</u> |
|--|---------------------|---------------------|
| [Distribution < DIRECTORY >                      |                     |                     |
| Blank.xls  | 03/17/2000          | 34,816              |
| BlankLibrary.xls                                 | 07/25/2001          | 70,144              |
| Getting Started.doc                              | 09/18/2001          | 41,472              |
| Quick Start.doc                                  | 09/14/2001          | 25,088              |
| SubtractionLibraryUtilityProgramUser'sManual.doc | 07/25/2001          | 190,976             |
| SubtractionLibraryUtility.exe                    | 07/25/2001          | 360,960             |
| TUTORIAL007.Seq                                  | 06/11/2001          | 604                 |
| TUTORIAL008.Seq                                  | 06/11/2001          | 632                 |
| TUTORIAL005.Seq                                  | 06/11/2001          | 684                 |
| TUTORIAL009.Seq                                  | 06/11/2001          | 647                 |
| TUTORIAL006.Seq                                  | 06/11/2001          | 686                 |
| TUTORIAL013.Seq                                  | 06/11/2001          | 1,188               |
| TUTORIAL017.Seq                                  | 06/11/2001          | 666                 |
| TUTORIAL020.Seq                                  | 06/11/2001          | 611                 |
| TUTORIAL010.Seq                                  | 06/11/2001          | 642                 |
| TUTORIAL014.Seq                                  | 06/11/2001          | 614                 |
| TUTORIAL018.Seq                                  | 06/11/2001          | 617                 |
| TUTORIAL011.Seq                                  | 06/11/2001          | 892                 |
| TUTORIAL015.Seq                                  | 06/11/2001          | 657                 |
| TUTORIAL019.Seq                                  | 06/11/2001          | 665                 |

|  |                   |              |
|--|-------------------|--------------|
| TUTORIAL012.Seq                          | 06/11/2001        | 619          |
| TUTORIAL016.Seq                          | 06/11/2001        | 641          |
| TUTORIAL005r.Seq                         | 06/11/2001        | 614          |
| TUTORIAL001.Seq                          | 06/11/2001        | 640          |
| TUTORIAL PRIMERS.VEC                     | 06/08/2001        | 2,039        |
| TUTORIAL002.Seq                          | 06/11/2001        | 643          |
| TUTORIAL003.Seq                          | 06/11/2001        | 627          |
| TUTORIAL004.Seq                          | 06/11/2001        | 682          |
| Source_code < DIRECTORY >                |                   |              |
| SubtractionLibraryUtility < DIRECTORY >] |                   |              |
| MakeHelp.bat                             | 09/27/2000        | 1,594        |
| newlibrarynamedlg.cpp                    | 10/05/2000        | 1,926        |
| newlibrarynamedlg.h                      | 09/29/2000        | 883          |
| resource.h                               | 02/06/2001        | 8,530        |
| resource.hm                              | 02/06/2001        | 4,528        |
| startdlg.cpp                             | 10/23/2000        | 3,742        |
| startdlg.h                               | 10/23/2000        | 1,093        |
| StdAfx.cpp                               | 10/11/2000        | 221          |
| StdAfx.h                                 | 10/03/2000        | 602          |
| SubtractionLibraryUtility.cpp            | 10/11/2000        | 4,047        |
| SubtractionLibraryUtility.h              | 02/06/2001        | 6,385        |
| [SubtractionLibraryUtility.mdp           | 09/11/2001        | 42,496]      |
| <u>Subtraction Library Utility.hpj</u>   | <u>02/06/2001</u> | <u>2,624</u> |
| SubtractionLibraryUtility.rc             | 07/25/2001        | 28,316       |
| SubtractionLibraryUtilityDlg.cpp         | 06/21/2001        | 209,771      |
| SubtractionLibraryUtilityDlg.h           | 04/16/2001        | 6,943        |
| <u>Subtraction Library Utility.hm</u>    | <u>08/09/2001</u> | <u>663</u>   |
| TimedMessage.cpp                         | 10/27/2000        | 1,718        |
| TimedMessage.h                           | 0/27/2000         | 875          |
| trimdialog.cpp                           | 11/06/2000        | 119,594      |
| trimdialog.h                             | 11/06/2000        | 4,099        |

[Hlp <DIRECTORY >

|                                       |                   |              |
|---------------------------------------|-------------------|--------------|
| AfxDlg.doc                            | 10/24/2000        | 276,992      |
| AfxDlg.rtf                            | 02/07/2001        | 4,284,257    |
| Copy of SubtractionLibraryUtility.hpj | 10/24/2000        | 2,637        |
| Copy of AfxDlg.rtf                    | 02/07/2001        | 4,284,257    |
| main.bmp                              | 10/13/2000        | 709,686      |
| MainScreen.bmp                        | 02/07/2001        | 718,454      |
| NewLibraryScreen.bmp                  | 10/27/2000        | 124,374      |
| oldAfxDlg.rtf                         | 02/07/2001        | 4,284,270    |
| start.bmp                             | 10/16/2000        | 219,798      |
| SubtractionLibraryUtility.cnt         | 09/27/2000        | 157          |
| SUBTRACTIONLIBRARYUTILITY.HLP         | 08/09/2001        | 2,115,387    |
| SubtractionLibraryUtility.hm          | 08/09/2001        | 663          |
| SubtractionLibraryUtility.hpj         | 02/06/2001        | 2,624        |
| SubtractionLibraryUtility.ph          | 09/27/2000        | 0            |
| trim.bmp                              | 10/16/2000        | 1,109,674    |
| TrimScreen.bmp                        | 10/27/2000        | 1,844,214    |
| word60AfxDlg.doc                      | 10/24/2000        | 2,171,392    |
| WorkingAfxDlg.rtf                     | 10/30/2000        | 7,246,340    |
| Res < DIRECTORY >                     |                   |              |
| SubtractionLibraryUtility.ico         | 06/11/2001        | 1,078        |
| SubtractionLibraryUtility.rc2         | 09/27/2000        | 417          |
| 67 Files Listed: 30,595,230 bytes]    |                   |              |
| <u>TUTORIAL PRIMERS.VEC</u>           | <u>06/08/2001</u> | <u>2,039</u> |
| <u>TUTORIAL001.Seq</u>                | <u>06/11/2001</u> | <u>640</u>   |

Paragraph at page 8, line 3, has been amended as follows:

#### BRIEF DESCRIPTION OF THE DRAWING

Fig. 1 shows a file directory structure for one embodiment of the invention.

Fig. 2 shows a Main User Interface computer display.

Fig. 3 (SEQ ID NOS 7, 9 and 12-16) shows a Trimming Interface computer display.

Table 2. beginning on page 18 has been amended as follows:

Table 2.

-----  
 Schlager's BLAST UTILITY, RESECO @1999  
 Results from file \\r5840\pub\MolTox\blast\TRIMMED\MB2D\M2r02\_NV.SEQ  
 BLAST search done 4/5/2000  
 -----

HTTP/1.0 200 OK MIME-Version: 1.0 Content-type: text/html

The query sequence for this search has been filtered. Filtering eliminates low complexity regions that commonly give spuriously high scores that reflect compositional bias rather than significant position-by-position alignment. Filtering can eliminate these potentially confounding matches (e.g., hits against proline-rich regions or poly-A tails) from the blast reports, leaving regions whose blast statistics reflect the specificity of their pairwise alignment.

BLASTN 2.0.11 [Jan-20-2000]

Reference: Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schaffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

Query= RESECO BLAST

UTILITY:\\r5840\pub\MolTox\blast\TRIMMED\MB2D\M2r02\_NV.SEQ  
 (561 letters)

Database: nt

607,850 sequences; 1,816,255,750 total letters  
 -----

|  | <u>Score</u> | <u>E</u> |
|--|--------------|----------|
| Sequences producing significant alignments:                    |              |          |
| gi 3228368 gb K02061.1 MUSRPL4A Mus musculus L32-4A pseudog... | 565          | e-159    |
| gi 6981481 ref NM_013226.1   Rattus norvegicus ribosomal pr... | 452          | e-125    |

-----  
 gi|3228368|gb|K02061.1|MUSRPL4A Mus musculus L32-4A pseudogene, complete seq  
 Length = 1516

Score = 565 bits (285), Expect = e-159

Identities = 360/384 (93%), Gaps = 5/384 (1%)

Strand = Plus / Minus

Query: SEQ ID NO: 1

38 gcagggtttgtgattttattttaaacataaaacatgcacacaagccatctactcattttct 97  
 |||

Sbjct: SEQ ID NO: 2

1094 gcagggtttgtgattttattttaaacataaaacatgcacacaagccatctattcattttct 1035  
 Query: 98 tcgctgcgtancctggcggttggtgactctgatggccagctgtgctgctctttct 157  
 |||

Sbjct: 1034 tcgctgcgtagcctggcggttggtgactctgatggccagctgtgctgctctttct 975  
 Query: 158 acaatggcttttcagttcttanaggacacattgtgagcaatctcagcacagtaagatttg 217  
 |||

Sbjct: 974 acaatggcttttcggttcttagaggacacattgtgagcaatctcagcacagtaagatttg 915  
 Query: 218 ttgcacatcagcagcacctccagctccttgacattgtggaccannaacttgcggaanccg 277

```

|||||
Sbjct: 914 ttgcacatcagcagcacctccagctccttgacattgtggaccaggaacttgcggaagccg 855
Query: 278 ctgggcagcatgtgcttgggttttcttgttgctcccaaacgaagtttnggcacangat 337
|||||
Sbjct: 854 ctgggcagcatgtgcttgggttttcttgttgctcccataaacgatg-ttgggcacagcat 796
Query: 338 ntggcccttgaaccttctcc-cncctgttgcnatgcctctgggtttccnc--atttcn 394
|||||
Sbjct: 795 ctggcccttgaaccttctccgcaccctgttgcnaatgcctctgggtttccgccagtttcg 736
Query: 395 cttaa-tttcccatatcggtctga 417
|||||
Sbjct: 735 ctttaattttcacatatcggtctga 712

```

gi|6981481|ref|NM\_013226.1|| Rattus norvegicus ribsml protein L32(Rpl32), mRNA

Length = 465

Score = 452 bits (228), Expect = e-125

Identities = 319/350 (91%), Gaps = 2/350 (0%)

Strand = Plus / Minus

Query: SEQ ID NO: 3

```

38 gcagggtttgtgattttattttaacataaaacatgcacacaagccatctactcattttct 97
|||||

```

Sbjct: SEQ ID NO: 4

```

461 gcagtttttgtggtttttatttgaacacaaaacaggcacacaagccatctattcatttctct 402
Query: 98 tcgctgcgtancctggcggttggtgactctgatggccagctgtgctgctctttct 157
|||||
Sbjct: 401 tcgctgcgtagcctggcggttggtgactctgatggccagctgtgctgctctttct 342
Query: 158 acaatggcttttcagttcttanaggacacattgtgagcaatctcagcacagtaagatttg 217
|||||
Sbjct: 341 acgatggcttttcggttcttagaggacacattgtgagcaatctcagcacagtaagatttg 282
Query: 218 ttgcacatcagcagcacctccagctccttgacattgtggaccannaacttgcggaanccg 277
|||||
Sbjct: 281 ttgcacatcagcagcacttccagctccttgacattgtggaccagaaacttccggaagccg 222
Query: 278 ctgggcagcatgtgcttgggttttcttgttgctcccaaacgaagtttnggcacangat 337
|||||
Sbjct: 221 ctaggcagcatgtgcttgggttttcttgttactcccgttaacc-aatgttgggcatcaggat 163
Query: 338 ntggcccttgaaccttctcc-cncctgttgcnatgcctctgggtttcc 386
|||||
Sbjct: 162 ctggcccttgaatcttctccgcaccctgttgcgatgcctctgggtttcc 113

```

Database: nt

Posted date: Mar 30, 2000 10:02 PM

Number of letters in database: 1,816,255,750

Number of sequences in database: 607,850

```

Lambda      K      H
1.37      0.711    0.00

```

Gapped

```

Lambda      K      H
1.37      0.711 4.94e-324

```

Matrix: blastn matrix:1 -3

Gap Penalties: Existence: 5, Extension: 2

Number of Hits to DB: 420761

Number of Sequences: 607850

Number of extensions: 420761

Number of successful extensions: 34073

Number of sequences better than 10.0: 52

length of query: 561  
 length of database: 1,816,255,750  
 effective HSP length: 20  
 effective length of query: 541  
 effective length of database: 1,804,098,750  
 effective search space: 976017423750  
 effective search space used: 976017423750  
 T: 0  
 A: 0  
 X1: 6 (11.9 bits)  
 X2: 10 (19.8 bits)  
 S1: 12 (24.3 bits)  
 S2: 19 (38.2 bits)

---

The label for Table 3. at page 20, line 8, has been amended as follows:

Table 3. (SEQ ID NO: 5)

The paragraph at page 24, line 7 has been amended as follows:

A vector file must be customized for a particular laboratory and selected prior to the trimming step. The vectors files are formatted using a six line, ASCII text format. Only the first contiguous string of letters on each line is read, so the remainder of each line can be used for annotations. Each line starts with a nucleotide sequence. An example vector file is presented below (SEQ ID NOS 6-11, respectively in order of appearance):

```

AGCGGCCCGCCCGGGCAGGTC // positive insertion orientation 5' adapter sequence
ACCTCGGCCGCGACCACGCT // positive insertion orientation 3' adapter sequence
TTACTAGTGGATCCGAGCTCGGTACCAAGCTTC // forward direction confirm
fragment 25 bases after 3' adapter
AGCGTGGTCGCGGCCGAGGT // negative insertion orientation 5' adapter sequence
ACCTGCCCCGGCGGCCGCTC // negative insertion orientation 3' adapter sequence
CACACTGGCGGCCGCTCGAGCATGCATCTAGAG // reverse direction confirm fragment
25 bases after 3' adapter.
  
```